REMARKS

The specification has been amended in several places to correct typographical errors. In the table, for compounds 4, 9, and 16, the point of substitution in the HetAr group was corrected. For compounds 18 and 32 in the same table, the spelling of pyrazine was corrected. Support for these amendments can be found, for example, in the list of named compounds on pages 19-21.

In the list of compounds on pages 19-21, the compound in paragraph starting on line 22 on Page 19 has been deleted because it is a duplicate. The compounds in paragraphs starting on line 28 on Page 19 to line 8 on page 20 have been amended to recite the proper substituent group isopropyl instead of methylpropyl. Support for this can be found in Table 1, compounds number 7 - 12.

In the list of compounds on pages 19-21, the compounds in the paragraphs starting on line 22 on Page 21 going to line 35 on page 21 have been amended to recite the proper substituent group 3,5-dimethylisothiazol. Support for this can be found in Table 1, compounds number 32 - 36.

Claim 1 has been amended to remove a redundant recitation of substituted amino substituents in order to more clearly point out what Applicant's consider to be their invention.

Claim 7 has been amended to correct a typographical error.

Claims 17 and 18 have been amended to remove improper dependence of a multiply dependent claim on a multiply dependent claim.

New Claims 19 to 29 have been added to replace matter that was removed by the amendments to Claims 17 and 18. Support can be found at least in Claims 17 and 18 as originally filed.

New Claim 25 is directed to specific compounds of the claimed invention, as listed in Applicant's specification starting on page 19 and in the examples starting on page 104.

No new matter has been introduced in the amended claims or in the newly added claims. Applicant's believe that the present amendments place this application in condition for allowance and request expedited examination and notice of allowance.

The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: November 22, 2002

By: Julie L. Heinrich
Julie L. Heinrich
Registration No. 48, 070

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

Attachment to Reply and Amendment dated October 30, 2002

Marked-up Copy

In the specification

The table on pages 17 - 19

Cpd #	A	HetAr
1	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
2	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
3	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
4	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-**[5]**2-yl
5	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
6	[2-$N(CH_3)_2$-5-CF_3CH_2]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
7	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
8	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
9	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	**[2]**3-(2,6-di-MeOPh)pyridazin-6-yl
10	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
11	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
12	[2-$N(CH_3)_2$-5-$(CH_3)_2CH$]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
13	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
14	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
15	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
16	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	**[2]**5-(2,6-di-MeOPh)pyrimidin-2-yl
17	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
18	[2-$N(CH_3)_2$-5-$(CH_3CH_2)_2CH$]-pyrimidin-4-yl	5-(2,6-di-MeOPh)**[pyriazin]**pyrazin-2-yl

Cpd #	A	HetAr
19	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
20	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
21	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
22	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
23	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
24	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isoxazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
25	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
26	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
27	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
28	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
29	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
30	[2-$N(CH_3)_2$-5-(1,3,5-tri-CH_3pyrazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
31	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
32	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
33	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
34	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
35	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
36	[2-$N(CH_3)_2$-5-(3,5-di-CH_3isothiazol-4-yl]pyrimidin-4-yl	5-(2,6-di-MeOPh)**[pyriazin]**<u>**pyrazin**</u>-2-yl

The deleted paragraph starting on line 22 on Page 19:

[*N*-(2-(N,N-dimethylamino)-5-(2-methylpropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine];

The paragraph starting on line 28 on Page 19:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

The paragraph starting on line 31 on Page 19:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

The paragraph starting on line 34 on Page 19:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

The paragraph starting on line 1 on Page 20:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

The paragraph starting on line 4 on Page 20:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

The paragraph starting on line 7 on Page 20:

N-(2-(N,N-dimethylamino)-5-(2-**[methylpropyl]**<u>**isopropyl**</u>)pyrimidin-4-yl)-L-3-(5**[2]**-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

The paragraph starting on line 22 on Page 21:

N-(2-(N,N-dimethylamino)-5-(**[1,3,5-trimethylpyrazol]**<u>**3,5-dimethylisothiazol**</u>-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

The paragraph starting on line 25 on Page 21:

N-(2-(N,N-dimethylamino)-5-(**[1,3,5-trimethylpyrazol]3,5-dimethylisothiazol**-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

The paragraph starting on line 28 on Page 21:

N-(2-(N,N-dimethylamino)-5-(**[1,3,5-trimethylpyrazol]3,5-dimethylisothiazol**-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

The paragraph starting on line 31 on Page 21:

N-(2-(N,N-dimethylamino)-5-(**[1,3,5-trimethylpyrazol]3,5-dimethylisothiazol**-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine; and

The paragraph starting on line 34 on Page 21:

N-(2-(N,N-dimethylamino)-5-(**[1,3,5-trimethylpyrazol]3,5-dimethylisothiazol**-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

The paragraph starting on line 16 on Page 88:

A mixture of a heteroaryl halide or heteroaryl triflate (1.0 eq.), an arylboronic acid (1.1 eq.), $CsCO_3$ (1.5 eq.), $Pd(PPh_3)_4$ (0.03 eq.) And anhydrous DMF was stirred under nitrogen at 100**[o]**°C for 48 h and then the DMF was evaporated. The residue was partitioned between ethyl acetate and half-saturated aqueous sodium chloride and then the ethyl acetate extracts were treated with magnesium sulfate, filtered and evaporated. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexanes to give the heteroaryl-aryl product.

The paragraph starting on line 8 on Page 90:

The desired dipeptide ester was prepared by the reaction of a carboxylic acid (1 equivalent) with the appropriate amino acid ester or amino acid ester hydrochloride (1 equivalent), benzotriazol-1-yloxy-tris(dimethylamino)phos-phonium hexafluorophosphate

[BOP] (2.0 equivalent), triethylamine (1.1 equivalent), and DMF. The reaction mixture was stirred at room temperature overnight. The crude product is purified by flash chromatography to afford the dipeptide ester.

The paragraph starting on line 2 on Page 104:

Synthesis of *N*-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2,**[5]6**-dimethoxyphenyl)-pyridin-2-yl)alanine

The paragraph starting on line 13 on Page 104:

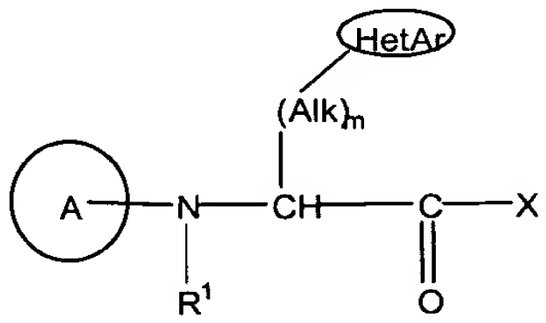
2,2,2-Trifluoroethyl **triflate** (prepared accordingly to Gassman, et al. J. Org. Chem., 1984, 49(12), 2258-2273) was converted via sequential application of methods Z, CC, and EE to give 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine. D.L-(5-(2,6-dimethoxyphenyl)pyridine-2-yl)alanine ethyl ester and 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine were coupled via method FF and the product was transformed via sequential application of methods GG and L to give the title compound.

The paragraph starting on line 1 on Page 105:

2,2,2-Trifluoroethyl **triflate** (prepared accordingly to Gassman, et al. J. Org. Chem., 1984, 49(12), 2258-2273) was converted via sequential application of methods Z, CC, and EE to give 4,6-dichloro-5-(2,2,2-trifluoroethyl) pyrimidine. D.L-(5-(2-methoxyphenyl)pyridine-2-yl)alanine ethyl ester and 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine were coupled via method FF and the product was transformed via sequential application of methods GG and L to give the title compound.

IN THE CLAIMS

1. (Amended) A compound of Formula (I):



(I)

wherein:

A is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-substituted aryl, $-OS(O)_2$-heteroaryl, $-OS(O)_2$-substituted heteroaryl, $-OS(O)_2$-heterocyclic, $-OS(O)_2$-substituted heterocyclic, $-OSO_2$-NRR where each R is independently hydrogen or alkyl, **[$-NRS(O)_2$-alkyl, $-NRS(O)_2$-substituted alkyl, $-NRS(O)_2$-aryl, $-NRS(O)_2$-substituted aryl, $-NRS(O)_2$-heteroaryl, $-NRS(O)_2$-substituted heteroaryl, $-NRS(O)_2$-heterocyclic, $-NRS(O)_2$-substituted heterocyclic,**]$-NRS(O)_2$-NR-alkyl, $-NRS(O)_2$-NR-substituted alkyl, $-NRS(O)_2$-NR-aryl, $-NRS(O)_2$-NR-substituted aryl, $-NRS(O)_2$-NR-heteroaryl, $-NRS(O)_2$-NR-substituted heteroaryl, $-NRS(O)_2$-NR-heterocyclic, $-NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, **[$-N[S(O)_2-R']_2$ and**]$-N[S(O)_2$-

NR'_2 where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HetAr is a nitrogen containing heteroaryl or a nitrogen containing substituted heteroaryl group;

Alk is an alkylene group of 1 to 4 carbons;

m is 0 or 1;

R^1 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR″R″ where each R″ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, **[diasteromers]**<u>**diastereomers**</u> and pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula (I) has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

7. (Amended) The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group is **[subsituted]**<u>**substituted**</u> with an aryl or substituted aryl group.

17. (Amended) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a

pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of **[Claims 1-16]**<u>**Claims 1 - 9, 11, or 12.**</u>

18. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of **[Claims 1-16]**<u>**Claims 1 - 9, 11, or 12.**</u>

19. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 10.

20. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 13.

21. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 14.

22. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of 15.

23. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 16.

24. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 10.

25. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 13.

26. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 14.

27. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 15.

28. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 16.

29. (New) A compound selected from the group consisting of

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-L-3-(52-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1-ethylpropyl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisoxazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(1,3,5-trimethylpyrazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2,5-dimethoxyphenyl)-pyridin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2-methoxyphenyl)-pyridin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(N,N-dimethylamino-carbonyloxy)-pyridin-2-yl)alanine;

N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(2-(N,N-dimethylamino-carbonyloxy)-pyridin-5-yl)alanine; and

pharmaceutically acceptable salts thereof.